L9 ANSWER 1 OF 2 PHIN COPYRIGHT 2009 Informa UK Ltd on STN

AN 2005:14312 PHIN
DED 19 Sep 2005
TI PHARMAPROJECTS - New Neurological Products for week ending 16 September 2005
SO Scrip-Online-plus (2005)
DT Newsletter
FS FULL

L9 ANSWER 2 OF 2 DRUGU COPYRIGHT 2009 THOMSON REUTERS on STN
AN 112843 DRUGU
FS Registry
DDRN DR0148914
DDN **ABT-769**
CT ANTICONVULSANTS; TRIAL-PREP.
SS AMINOACID; C-AMIDE; CYCLOPROPANE; SPIRO; CYCLOHEXANE

=> dup rem
ENTER L# LIST OR (END):l7
DUPLICATE IS NOT AVAILABLE IN 'ADISINSIGHT, ADISNEWS, DGENE, DRUGMONOG2, IMSPRODUCT, KOSMET, NUTRACEUT, PCTGEN, PHARMAML, USGENE'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L7
L10 5 DUP REM L7 (13 DUPLICATES REMOVED)

=> d l10 1-5 ibib, kwic

L10 ANSWER 1 OF 5 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
DUPLICATE 1
ACCESSION NUMBER: 2005:510269 BIOSIS
DOCUMENT NUMBER: PREV200510298067
TITLE: Preclinical profiling and safety studies of **ABT-769**: A compound with potential for broad-spectrum antiepileptic activity.
AUTHOR(S): Giardina, William J.; Dart, Michael J.; Harris, Richard R.; Bitner, Robert S.; Radek, Richard J.; Fox, Gerard B.; Chemburkar, Sanjay R.; Marsh, Kennan C.; Waring, Jeffrey F.; Hui, Julia Y; Chen, Jinhua; Curzon, Peter; Grayson, George K.; Komater, Victoria A.; Ku, Yiyin; Lockwood, Mark; Miner, Holly M.; Nikkel, Arthur L.; Pan, Jia Bao; Pu, Yu-Ming; Wang, Lei; Bennani, Youssef; Durmuller, Niklaus; Jolly, Robert; Sullivan, James P.; Roux, Sylvain; Decker, Michael W. [Reprint Author]
CORPORATE SOURCE: Abbott Labs, Dept R4N5, Bldg AP 9A-3,100 Abbott Pk Rd, Abbott Pk, IL 60064 USA
michael.w.decker@abbott.com
SOURCE: Epilepsia, (SEP 2005) Vol. 46, No. 9, pp. 1349-1361.
CODEN: EPILAK. ISSN: 0013-9580.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Nov 2005
Last Updated on STN: 23 Nov 2005
TI Preclinical profiling and safety studies of **ABT-769**: A compound with potential for broad-spectrum antiepileptic activity.
AB Purpose: The objective of this study was to characterize the antiseizure and safety profiles of **ABT-769** [(R)-N-(2 amino-2-oxoethyl)spiro[2,5]octane-1-carboxamide].Methods: **ABT-**

769 was tested for protection against maximal electroshock and pentylenetetrazol-induced **seizures** in the mouse and for suppression of electrically kindled amygdala **seizures** and spontaneous absence-like **seizures** in the rat. The central nervous system safety profile was evaluated by using tests of motor coordination and inhibitory avoidance.. . . toxicity was assessed in vitro by using a mitochondrial fatty acid beta-oxidation assay. Teratogenic potential was assessed in the mouse.Results: **ABT-769** blocked maximal electroshock, subcutaneous pentylenetetrazol and intravenous pentylenetetrazol-induced **seizures** with median effective dose (ED50) values of 0.25, 0.38, and 0.11 mmol/kg, p.o., respectively. No tolerance was evident in the intravenous pentylenetetrazol test after twice-daily dosing of **ABT-769** (0.3 mmol/kg, p.o.) for 4 days. **ABT-769** blocked absence-like spike-wave discharge (ED50, 0.15 mmol/kg, p.o.) and shortened the cortical and amygdala afterdischarge duration of kindled **seizures** (1 and 3 mmol/kg, p.o.). The protective indices (ED50 rotorod impairment/ED50 **seizure** protection) were 4.8, 3.2, and 10.9 in the maximal electroshock, subcutaneous pentylenetetrazol and intravenous pentylenetetrazol **seizure** tests, respectively. **ABT-769** did not affect inhibitory avoidance performance (0.1-1 mmol/kg, p.o.). **ABT-769** did not affect mitochondrial fatty acid beta-oxidation or induce neural tube defects.Conclusions: **ABT-769** is an efficacious antiseizure agent in animal models of **convulsive** and nonconvulsive **epilepsy** and has a favorable safety profile. **ABT-769** has a broad-spectrum profile like that of valproic acid. Its profile is clearly different from those of carbamazepine, phenytoin, lamotrigine,. . .

IT . . .
Toxicology; Nervous System (Neural Coordination)

IT Parts, Structures, & Systems of Organisms
liver: digestive system; amygdala: nervous system

IT Diseases
seizure: nervous system disease, drug therapy, chemically-induced, pathology
Seizures (MeSH)

IT Chemicals & Biochemicals
fatty acid; pentylenetetrazol: toxin; **ABT-769** [[(R)- N-(2 amino-2-oxoethyl)spiro[2,5]octane-1-carboxamide]]: anticonvulsant-drug, pharmacodynamics, safety, efficacy, adverse effects, dosage; valproic acid: central depressant-drug, tranquilizer-drug, anticonvulsant-drug, enzyme inhibitor-drug

L10 ANSWER 2 OF 5 Elsevier Biobase COPYRIGHT 2009 Elsevier Science B.V. on STN

ACCESSION NUMBER: 2006175004 ESBIOBASE

TITLE: Preclinical profiling and safety studies of **ABT-769**: A compound with potential for broad-spectrum antiepileptic activity

AUTHOR(S): Giardina, William J.; Dart, Michael J.; Harris, Richard R.; Bitner, Robert S.; Radek, Richard J.; Fox, Gerard B.; Chemburkar, Sanjay R.; Marsh, Kennan C.; Waring, Jeffrey F.; Hui, Julia Y; Chen, Jinhua; Curzon, Peter; Grayson, George K.; Komater, Victoria A.; Ku, Yiyin; Lockwood, Mark; Miner, Holly M.; Nikkel, Arthur L.; Pan, Jia Bao; Pu, Yu-Ming; Wang, Lei; Bennani, Youssef; Jolly, Robert; Sullivan, James P.; Decker, Michael W.; Durmuller, Niklaus; Roux, Sylvain

CORPORATE SOURCE: Giardina, William J.; Dart, Michael J.; Harris, Richard

10691095

R.; Bitner, Robert S.; Radek, Richard J.; Fox, Gerard B.; Chemburkar, Sanjay R.; Marsh, Kennan C.; Waring, Jeffrey F.; Hui, Julia Y; Chen, Jinhua; Curzon, Peter; Grayson, George K.; Komater, Victoria A.; Ku, Yiyin; Lockwood, Mark; Miner, Holly M.; Nikkel, Arthur L.; Pan, Jia Bao; Pu, Yu-Ming; Wang, Lei; Bennani, Youssef; Jolly, Robert; Sullivan, James P.; Decker, Michael W. (Global Pharmaceutical Research and Development, Abbott Laboratories, Abbott Park, IL (US)); Bennani, Youssef (Vertex Pharmaceuticals, Cambridge, MA 01239 (US)); Jolly, Robert (Lilly Research Labs., Greenfield, IN 46104 (US)); Decker, Michael W. (Neuroscience Research, Department R4N5, Abbott Laboratories, 100 Abbott Park Road, Abbott Park, IL 60064-6125 (US)); Durmuller, Niklaus; Roux, Sylvain (Porsolt and Partners Pharmacology, Le Genest-Saint-Isle (FR))
EMAIL: michael.w.decker@abbott.com
SOURCE: Epilepsia (Sep 2005) Volume 46, Number 9, pp. 1349-1361, 33 refs.
CODEN: EPILAK ISSN: 0013-9580 E-ISSN: 1528-1167
DOI: 10.1111/j.1528-1167.2005.02905.x
COUNTRY OF PUBLICATION: United States of America
DOCUMENT TYPE: Journal; Article
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 3 Feb 2009
Last updated on STN: 3 Feb 2009

Preclinical profiling and safety studies of **ABT-769**: A compound with potential for broad-spectrum antiepileptic activity

ST **Absence seizures**; **ABT-769**; **Animal seizure models**; Anticonvulsant drugs; **Kindled amygdala seizures**; Maximal electroshock; Pentylenetetrazol; Valproic acid

AB Purpose: The objective of this study was to characterize the antiseizure and safety profiles of **ABT-769** [(R)-N-(2 amino-2-oxoethyl)spiro[2,5]octane-1- carboxamide]. Methods: **ABT-769** was tested for protection against maximal electroshock and pentylenetetrazol-induced **seizures** in the mouse and for suppression of electrically kindled amygdala **seizures** and spontaneous absence-like **seizures** in the rat. The central nervous system safety profile was evaluated by using tests of motor coordination and inhibitory avoidance.. . . was assessed in vitro by using a mitochondrial fatty acid β-oxidation assay. Teratogenic potential was assessed in the mouse. Results: **ABT-769** blocked maximal electroshock, subcutaneous pentylenetetrazol and intravenous pentylenetetrazol-induced **seizures** with median effective dose (ED 50) values of 0.25, 0.38, and 0.11 mmol/kg, p.o., respectively. No tolerance was evident in the intravenous pentylenetetrazol test after twice-daily dosing of **ABT-769** (0.3 mmol/kg, p.o.) for 4 days. **ABT-769** blocked absence-like spike-wave discharge (ED 50 , 0.15 mmol/kg, p.o.) and shortened the cortical and amygdala afterdischarge duration of kindled **seizures** (1 and 3 mmol/kg, p.o.). The protective indices (ED 50 rotorod impairment/ED 50 **seizure** protection) were 4.8, 3.2, and 10.9 in the maximal electroshock, subcutaneous pentylenetetrazol and intravenous pentylenetetrazol **seizure** tests, respectively. **ABT-769** did not affect inhibitory avoidance performance (0.1-1 mmol/kg, p.o.). **ABT-769** did not affect mitochondrial fatty acid β-oxidation or induce neural tube defects. Conclusions: **ABT-769** is an efficacious antiseizure agent in animal models of **convulsive**

and nonconvulsive **epilepsy** and has a favorable safety profile. **ABT-769** has a broad-spectrum profile like that of valproic acid. Its profile is clearly different from those of carbamazepine, phenytoin, lamotrigine, topiramate, vigabatrin, and tiagabine. .COPYRGT. 2005 International League Against **Epilepsy** .

L10 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2004:857165 CAPLUS
DOCUMENT NUMBER: 141:325759
TITLE: Spirocyclopropyl amides and acids and their therapeutic applications
INVENTOR(S): Bennani, Youseff L.; Bunnelle, William H.; Chang, Sou-Jen; Chemburkar, Sanjay R.; Chen, Jinhua; Dart, Michael J.; Fernando, Dilinie; Ku, Yi-Yin; Lockwood, Mark; Wang, Lei
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 27 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 20040204396	A1	20041014	US 2003-691095		20031022
PRIORITY APPLN. INFO.:			US 2002-420286P	P	20021022

OTHER SOURCE(S): MARPAT 141:325759
AB . . . = H, alkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heterocycle, heterocyclealkyl; R3, R4 = H, alkenyl, alkyl, etc.) for the treatment of **epilepsy**, bipolar disorder, psychiatric disorders, migraine, pain, or movement disorders, and to provide neuroprotection. Representative compds. exhibited anticonvulsant ED50s in the. . .
ST . . . treatment spirocyclopropyl acid amide; psychiatric disorder treatment spirocyclopropyl amide acid; pain treatment spirocyclopropyl amide acid; migraine treatment spirocyclopropyl amide acid; **epilepsy** treatment spirocyclopropyl amide acid
IT Mental and behavioral disorders
(bipolar disorder, treatment of; spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)
IT Headache
(migraine, treatment of; spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)
IT Nerve, disease
(neuropathy, pain, treatment of; spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)
IT Cytoprotective agents
Nervous system agents
(neuroprotective agents; spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)
IT Inflammation
(pain, treatment of; spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)
IT Drug delivery systems

(prodrugs; spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)

IT Analgesics
Anticonvulsants
Antimigraine agents
Mammalia
(spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)

IT **Epilepsy**
Mental and behavioral disorders
Movement disorders
Pain
(treatment of; spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)

IT 17202-86-7P, Spiro[2.5]octane-1-carboxylic acid 17202-94-7P, Spiro[2.4]heptane-1-carboxylic acid 680618-92-2P, (1S)-N-((1S)-2-Amino-1-methyl-2-oxoethyl)spiro[2.5]octane-1-carboxamide 680618-93-3P, (1R)-N-((1S)-2-Amino-1-methyl-2-oxoethyl)spiro[2.5]octane-1-carboxamide 680618-94-4P 680618-96-6P 680618-99-9P 680619-02-7P, 2-Methylspiro[2.5]octane-1-carboxylic acid 680619-04-9P, 5,7-Dimethylspiro[2.5]octane-1-carboxylic acid 680619-06-1P, 6-tert-Butylspiro[2.5]octane-1-carboxylic acid 680619-08-3P, 2-Methylspiro[2.4]heptane-1-carboxylic acid 680619-11-8P, 3,3-Dimethylspiro[bicyclo[2.2.1]heptane-2,1'-cyclopropane]-2'-carboxylic acid 680619-14-1P, 4-Methylspiro[bicyclo[3.2.0]heptane-6,1'-cyclopropane]-2'-carboxylic acid 680619-21-0P, Spiro[2.6]nonane-1-carboxylic acid 680619-24-3P 680619-30-1P 680619-41-4P, 5,5,7,7-Tetramethylspiro[2.5]octane-1-carboxylic acid 680619-52-7P, Spiro[bicyclo[3.2.0]heptane-6,1'-cyclopropane]-2'-carboxylic acid
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)

IT 680619-19-6, Spiro[bicyclo[2.2.1]heptane-2,1'-cyclopropane]-2'-carboxamide 680619-22-1, Spiro[2.6]nonane-1-carboxamide
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)

IT 17202-88-9P, Spiro[2.5]octane-1-carboxamide 17202-96-9P, Spiro[2.4]heptane-1-carboxamide 680618-91-1P, N-(2-Amino-2-oxoethyl)spiro[2.5]octane-1-carboxamide 680618-95-5P, (1S)-N-(2-Amino-2-oxoethyl)spiro[2.5]octane-1-carboxamide 680618-98-8P, N-(2-Amino-2-oxoethyl)spiro[2.4]heptane-1-carboxamide 680619-00-5P 680619-01-6P 680619-03-8P, N-(2-Amino-2-oxoethyl)-2-methylspiro[2.5]octane-1-carboxamide 680619-05-0P, N-(2-Amino-2-oxoethyl)-5,7-dimethylspiro[2.5]octane-1-carboxamide 680619-07-2P, N-(2-Amino-2-oxoethyl)-6-tert-butylspiro[2.5]octane-1-carboxamide 680619-09-4P, 2-Methylspiro[2.4]heptane-1-carboxamide 680619-10-7P, N-(2-Amino-2-oxoethyl)-2-methylspiro[2.4]heptane-1-carboxamide 680619-13-0P, N-(2-Amino-2-oxoethyl)-3,3-dimethylspiro[bicyclo[2.2.1]heptane-2,1'-cyclopropane]-2'-carboxamide 680619-16-3P, 4-Methylspiro[bicyclo[3.2.0]heptane-6,1'-cyclopropane]-2'-carboxamide 680619-17-4P, N-(2-Amino-2-oxoethyl)-4-methylspiro[bicyclo[3.2.0]heptane-6,1'-cyclopropane]-2'-carboxamide 680619-18-5P, Spiro[bicyclo(2.2.1)heptane-2,1'-cyclopropane]-2'-carboxylic

acid 680619-20-9P, N-(2-Amino-2-oxoethyl)spiro(bicyclo[2.2.1]heptane-2,1'-cyclopropane)-2'-carboxamide 680619-23-2P, N-(2-Amino-2-oxoethyl)spiro[2.6]nonane-1-carboxamide 680619-26-5P 680619-28-7P 680619-33-4P 680619-35-6P 680619-37-8P, N-(3-Amino-3-oxopropyl)spiro[2.5]octane-1-carboxamide 680619-43-6P, 5,5,7,7-Tetramethylspiro[2.5]octane-1-carboxamide 680619-45-8P, N-(2-Amino-2-oxoethyl)-5,5,7,7-tetramethylspiro[2.5]octane-1-carboxamide 680619-47-0P, [(Spiro[2.5]oct-1-ylcarbonyl)amino]acetic acid 680619-53-8P, N-(2-Amino-2-oxoethyl)spiro(bicyclo[3.2.0]heptane-6,1'-cyclopropane)-2'-carboxamide 680619-54-9P, (1R)-N-((2R)-2-Hydroxypropyl)spiro[2.5]octane-1-carboxamide 680619-55-0P, (1S)-N-((2R)-2-Hydroxypropyl)spiro[2.5]octane-1-carboxamide 680619-56-1P, (1R)-N-((2S)-2-Hydroxypropyl)spiro[2.5]octane-1-carboxamide 680619-57-2P, (1S)-N-((2S)-2-Hydroxypropyl)spiro[2.5]octane-1-carboxamide
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)

IT **680618-97-7**, (1R)-N-(2-Amino-2-oxoethyl)spiro[2.5]octane-1-carboxamide 680619-12-9, 3,3-Dimethylspiro[bicyclo[2.1.1]heptane-2,1'-cyclopropane]-2'-carboxamide 680619-39-0, Spiro[2.7]decane-1-carboxylic acid 680619-58-3 680619-59-4 680619-60-7, 2-Methylspiro[2.5]octane-1-carboxamide 680619-61-8, 5,7-Dimethylspiro[2.5]octane-1-carboxamide 680619-62-9, 6-tert-Butylspiro[2.5]octane-1-carboxamide 680619-63-0, Spiro[2.7]decane-1-carboxamide 680619-64-1, N-(2-Amino-2-oxoethyl)spiro[2.7]decane-1-carboxamide 680619-65-2, Spiro[bicyclo[3.2.0]heptane-6,1'-cyclopropane]-2'-carboxamide
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)

IT 623-73-4, Ethyl diazoacetate 1192-37-6, Methylenecyclohexane 1336-21-6, Ammonium hydroxide 1668-10-6, 2-Aminoacetamide hydrochloride 2799-16-8, (R)-1-Amino-2-propanol 2799-17-9, (S)-1-Amino-2-propanol 4726-85-6, 3-Aminopropanamide 4832-17-1, 2-Decalone 5680-79-5, Glycine methyl ester hydrochloride 33208-99-0, (2S)-2-Aminopropanamide hydrochloride 33883-43-1 110253-44-6 646990-40-1 770728-66-0 770728-67-1 770728-68-2 770728-69-3 770728-70-6 770728-71-7 770728-72-8 770728-74-0 770728-75-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)

IT 17202-87-8P 58396-40-0P, 2-Methylenedecahydronaphthalene 770728-73-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)

L10 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2004:331780 CAPLUS
DOCUMENT NUMBER: 140:338974
TITLE: Preparation of spirocyclopropyl amides and acids as anticonvulsants
INVENTOR(S): Bennani, Youssef L.; Bunnelle, William H.; Chang, Sou-Jen; Chemburkar, Sanjay R.; Chen, Jinhua; Dart, Michael J.; Fernando, Dilinie P.; Ku, Yi-Yin; Lockwood, Mark; Wang, Lei
PATENT ASSIGNEE(S): USA

10691095

SOURCE: U.S. Pat. Appl. Publ., 27 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040077616	A1	20040422	US 2002-277266	20021022
CA 2502906	A1	20040506	CA 2003-2502906	20031022
WO 2004037240	A1	20040506	WO 2003-US33688	20031022
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003283011	A1	20040513	AU 2003-283011	20031022
EP 1558230	A1	20050803	EP 2003-774943	20031022
EP 1558230	B1	20081231		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006513156	T	20060420	JP 2004-547101	20031022
AT 418973	T	20090115	AT 2003-774943	20031022
MX 2005004267	A	20050726	MX 2005-4267	20050421

PRIORITY APPLN. INFO.: US 2002-277266 A 20021022
WO 2003-US33688 W 20031022

OTHER SOURCE(S): MARPAT 140:338974

AB . . . saponified to give II. Representative examples of I exhibit ED50 = 0.84 - 0.35 mmol/kg in the s.c. pentylenetetrazole (PTZ) **seizure** model. I are useful in the treatment of **epilepsy**, bipolar disorder, psychiatric disorders, migraine, pain, or movement disorders, and to provide neuroprotection.

IT Analgesics
Anti-inflammatory agents
Anticonvulsants
Antimigraine agents
Epilepsy
Human
Pain
(preparation of spirocyclopropyl amides and acids as anticonvulsants)

IT 17202-88-9P, Spiro[2.5]octane-1-carboxamide 17202-96-9P, Spiro[2.4]heptane-1-carboxamide 680618-95-5P, (1S)-N-(2-Amino-2-oxoethyl)spiro[2.5]octane-1-carboxamide **680618-97-7P**, (1R)-N-(2-Amino-2-oxoethyl)spiro[2.5]octane-1-carboxamide 680618-98-8P, N-(2-Amino-2-oxoethyl)spiro[2.4]heptane-1-carboxamide 680619-00-5P 680619-01-6P 680619-03-8P, N-(2-Amino-2-oxoethyl)-2-methylspiro[2.5]octane-1-carboxamide 680619-05-0P, N-(2-Amino-2-oxoethyl)-5,7-dimethylspiro[2.5]octane-1-carboxamide 680619-07-2P, N-(2-Amino-2-oxoethyl)-6-tert-butylspiro[2.5]octane-1-carboxamide 680619-09-4P, 2-Methylspiro[2.4]heptane-1-carboxamide 680619-10-7P, N-(2-Amino-2-oxoethyl)-2-methylspiro[2.4]heptane-1-carboxamide 680619-12-9P, 3,3-Dimethylspiro[bicyclo[2.2.1]heptane-2,1'-cyclopropane]-2'-carboxamide 680619-13-0P, N-(2-Amino-2-oxoethyl)-3,3-

dimethylspiro[bicyclo[2.2.1]heptane-2,1'-cyclopropane]-2'-carboxamide 680619-16-3P, 4-Methylspiro[bicyclo[3.2.0]heptane-6,1'-cyclopropane]-2'-carboxamide 680619-17-4P, N-(2-Amino-2-oxoethyl)-4-methylspiro[bicyclo[3.2.0]heptane-6,1'-cyclopropane]-2'-carboxamide 680619-19-6P, Spiro[bicyclo[2.2.1]heptane-2,1'-cyclopropane]-2'-carboxamide 680619-20-9P, N-(2-Amino-2-oxoethyl)spiro[bicyclo[2.2.1]heptane-2,1'-cyclopropane]-2'-carboxamide 680619-22-1P, Spiro[2.6]nonane-1-carboxamide 680619-23-2P, N-(2-Amino-2-oxoethyl)spiro[2.6]nonane-1-carboxamide 680619-26-5P 680619-28-7P 680619-33-4P 680619-35-6P 680619-37-8P, N-(3-Amino-3-oxopropyl)spiro[2.5]octane-1-carboxamide 680619-43-6P, 5,5,7,7-Tetramethylspiro[2.5]octane-1-carboxamide 680619-45-8P, N-(2-Amino-2-oxoethyl)-5,5,7,7-tetramethylspiro[2.5]octane-1-carboxamide 680619-47-0P, [(Spiro[2.5]oct-1-ylcarbonyl)amino]acetic acid 680619-49-2P, (S)-[[Spiro[2.5]oct-1-ylcarbonyl]amino]acetic acid 680619-51-6P, (R)-[[Spiro[2.5]oct-1-ylcarbonyl]amino]acetic acid 680619-53-8P, N-(2-Amino-2-oxoethyl)spiro[bicyclo[3.2.0]heptane-6,1'-cyclopropane]-2'-carboxamide 680619-54-9P, (1R)-N-((2R)-2-Hydroxypropyl)spiro[2.5]octane-1-carboxamide 680619-55-0P, (1S)-N-((2R)-2-Hydroxypropyl)spiro[2.5]octane-1-carboxamide 680619-56-1P, (1R)-N-((2S)-2-Hydroxypropyl)spiro[2.5]octane-1-carboxamide 680619-57-2P, (1S)-N-((2S)-2-Hydroxypropyl)spiro[2.5]octane-1-carboxamide 680619-58-3P, (S)-Spiro[2.5]octane-1-carboxamide 680619-59-4P, (R)-Spiro[2.5]octane-1-carboxamide 680619-60-7P, 2-Methylspiro[2.5]octane-1-carboxamide 680619-61-8P, 5,7-Dimethylspiro[2.5]octane-1-carboxamide 680619-62-9P, 6-tert-Butylspiro[2.5]octane-1-carboxamide 680619-63-0P, Spiro[2.7]decane-1-carboxamide 680619-64-1P, N-(2-Amino-2-oxoethyl)spiro[2.7]decane-1-carboxamide 680619-65-2P, Spiro[bicyclo[3.2.0]heptane-6,1'-cyclopropane]-2'-carboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of spirocyclopropyl amides and acids as anticonvulsants)

L10 ANSWER 5 OF 5 ADISINSIGHT COPYRIGHT (C) 2009 Adis Data Information BV on STN
CN Research programme: antiepileptic therapies - Abbott Laboratories
CN **ABT 769; ABT-769**
CN (R)-N-(2-Amino-2-oxoethyl)spiro(2,5)octane-1-carboxamide
CC EPHMRA ATC CODE: **N3A Anti-Epileptics**
CC WHO ATC CODE: N03A-G Fatty acid derivatives
DSTA Preclinical, United States, **Epilepsy**
. . . antiepileptic therapies which have a better safety and tolerability profile than the current generation of drugs, the lead compound is **ABT 769** a valproic acid analogue with possible broad spectrum applications. The glycinamide moiety of **ABT 769**, in analogy with the nonteratogenic valproic acid derivative TV-1901 was incorporated into **ABT 769** to increase antiseizure efficacy and reduce the likelihood for induction of neural tube defects/1/.

TX Adverse Events:
Animal studies: in a preclinical study using mice and rats **ABT 769** showed a favourable safety profile. **ABT 769** did not affect mitochondrial fatty acid -oxidation or induce neural tube defects. Dosages of 4 and 8 mmol/kg od were. . .

TX PHARMACOLOGY:
Pharmacodynamics (**Epilepsy** and **Seizure** Disorders):

10691095

Animal studies: **ABT 769** was an efficacious antiseizure agent in animal models of **convulsive** and nonconvulsive **epilepsy**. **ABT 769** was tested for protection against maximal electroshock and pentylenetetrazol-induced **seizures** in the mouse, as well as suppression of electrically kindled amygdala **seizures** and spontaneous absense-like **seizures** in rats. **ABT 769** blocked maximal electroshock, subcutaneous pentylenetetrazol and IV pentylenetetrazol-induced **seizures** with ED sub(50) values of 0.25, 0.38 and 0.11 mmol/kg PO respectively. No tolerance was evident in the IV pentylenetetrazol test after bid dosing of **ABT 769** at 0.3 mmol/kg PO for four-days. **ABT 769** blocked absense like spike-wave discharge at an ED sub(50) value of 0.15 mmol/kg, and shortened the cortical and amygdala after-discharge duration of kindled **seizures** at ED sub(50) values of 1 and 3 mmol/ kg PO, repectively). **ABT 769** did not affect inhibitory avoidance performance at 0.1-1 mmol/kg PO/1/.

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(FILE 'HOME' ENTERED AT 14:34:42 ON 09 JUN 2009)

FILE 'REGISTRY' ENTERED AT 14:34:56 ON 09 JUN 2009
L1 1 S ABT 769/CN

FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CAPLUS, DDFB, DGENE, DISSABS, DRUGB, DRUGMONOG2, DRUGU, EMBAL, EMBASE, ESBIOBASE, IFIPAT, IMSDRUGNEWS, IMSPRODUCT, IPA, KOSMET, LIFESCI, MEDLINE, NAPRALERT, NLDB, NUTRACEUT, PASCAL, PCTGEN, PHARMAML, ...' ENTERED AT 14:35:15 ON 09 JUN 2009
L2 20 S L1 OR ABT 769
L3 772019 S EPILEP?
L4 228807 S CONVULS?
L5 581577 S SEIZURE
L6 1189744 S L3 OR L4 OR L5
L7 18 S L6 AND L2
L8 2 S L2 NOT L7
L9 2 DUP REM L8 (0 DUPLICATES REMOVED)
L10 5 DUP REM L7 (13 DUPLICATES REMOVED)

Jagoe